IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AFFYMETRIX, INC., a Delaware corporation, Plaintiff/Counter-Defendant, v. **ILLUMINA, INC.**, a Delaware corporation, Defendant/Counter-Plaintiff.	Civil Action No.: 04-901 JJF **PUBLIC VERSION**

OPENING BRIEF IN SUPPORT OF ILLUMINA'S MOTION FOR SUMMARY JUDGMENT OF INVALIDITY OF THE ASSERTED CLAIMS OF THE '432 PATENT

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NATURE AND STAGE OF THE PROCEEDINGS

Plaintiff Affymetrix, Inc. ("Affymetrix") filed suit against Defendant Illumina, Inc. ("Illumina") on July 26, 2004. (D.I. 1) In its complaint, Affymetrix accuses Illumina of infringing U.S. Patent Nos. 5,545,531; 5,795,716; 6,355,432; 6,399,365; 6,607,887; and 6,646,243. Illumina filed its Answer and Counterclaims denying, *inter alia*, that its products infringe and counterclaiming that the asserted patents are invalid under 35 U.S.C. §§ 102, 103 and 112. (D.I. 10) Illumina obtained leave to file and filed its Amended Answer and Counterclaims on February 17, 2006, adding, *inter alia*, allegations of unenforceability due to inequitable conduct. (D.I. 217) Subsequently, Affymetrix dismissed with prejudice one of the asserted patents -- U.S. Patent No. 6,607,887 -- from the litigation.[1] (D.I. 266)

The parties have completed fact discovery and *Markman* briefing on disputed claim terms of the patents-in-suit. The parties will proceed with expert discovery following a claim construction ruling from the Court.

SUMMARY OF THE ARGUMENT

Regardless of how the Court construes the claims of the '432 patent, the prior art poster abstract of two Yugoslavian scientists was published and publicly-available in this country more than one year before the filing date of the '432 patent and discloses each and every limitation of these claims. The '432 patent is thus invalid as a matter of law.

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[1] Weeks after discovery closed, Affymetrix attempted for the first time to assert additional patent claims, *inter alia*, claims 10, 21, and 22 of U.S. Pat. No. 6,355,432. (D.I. 235) Illumina has objected to Affymetrix's belated attempt to add new patent claims after fact discovery has closed, and letters by both parties have been submitted, pending a decision by this Court. (D.I. 235, 237, 238) Accordingly, this brief will not address the claims of the '432 patent that Affymetrix has belatedly sought to add — claims 10, 21, and 22 — although, for the same reasons as explained in this brief, these claims are also invalid as anticipated by the prior art. If the Court permits Affymetrix's belated addition of these claims, Illumina requests the opportunity to seek a summary judgment ruling that such claims are also invalid under 35 U.S.C. § 102.

Yugoslavian scientists Radomir Crkvenjakov and Radoje Drmanac presented a poster at two key scientific conferences in October and early November 1989 that describes their encoded bead array technology and sets forth all of the limitations of claims 2, 5, 8, and 9 of the '432 patent.[2] Numerous attendees at these conferences (including a member of Affymetrix's Scientific Advisory Board) verified that the poster abstracts were published and the posters were presented more than one year before the '432 patent claims were filed, and further confirmed the anticipatory nature of the technology disclosed in them. No question of material fact exists as to whether Drs. Crkvenjakov and Drmanac's poster abstract discloses each and every limitation of the asserted claims, and therefore the Court should grant Illumina's motion for summary judgment of invalidity pursuant to 35 U.S.C. § 102.

STATEMENT OF FACTS

I. The '432 Patent

On June 2, 2000, Drs. Stephen Fodor, Dennis Solas, and William Dower of Affymetrix filed a patent application entitled "Products for Detecting Nucleic Acids." This application issued as U.S. Pat. No. 6,355,432 (the '432 patent) on March 12, 2002. (Ex. A) Affymetrix contends that the '432 patent is entitled to claim priority back to U.S. Patent Application No. 07/624,114, which was filed on December 6, 1990. The '432 patent purports to teach an improved method on making and using a substrate for sequencing, fingerprinting, and mapping biological polymers, or specifically, nucleic acid molecules (DNA or RNA). The '432 patent describes a substrate of positionally defined polymers synthesized by a lithographic

[2] While the parties are in dispute over the '432 patent terms "target specific sequence" and "said beads being coded with an encoding system," Drs. Crkvenjakov and Drmanac's poster abstract disclosure anticipates these limitations under either party's proposed constructions. (*See* Illumina's Opening *Markman* Br. at 15-20 (D.I. 240); Affymetrix's Claim Construction Br. at 10-15 (D.I. 243))

process, trademarked by Affymetrix as the VLSIPS™ (Very Large Scale Immobilized Polymer Synthesis) technology. ('432 col. 2:29-49)

Affymetrix has asserted claims 2, 5, 8, and 9. Independent claim 1 (reproduced below), from which claim 2 depends, identifies the specific limitations of the claimed invention that include a plurality of beads with polymers of specific sequences attached. The beads are encoded so that the sequence attached to each bead can be determined:

> 1. A collection of beads comprising a plurality of beads which have binding polymers of different target specific sequence attached thereto; said beads being coded with an encoding system whereby the target specific sequence of the polymer attached to the beads can be identified.

('432 claim 1; *see also* Affymetrix's Claim Construction Br. at 6 (D.I. 243)) Claim 2 (reproduced below), from which all the relevant claims further depend, limits the polymers in the collection of claim 1 to short pieces of nucleic acids, called oligonucleotides:

> 2. The collection of claim 1, wherein the binding polymer is an oligonucleotide having a given length and is selected from the group consisting of all possible oligonucletide sequences having t he same number of nucleotides.

('432 claim 2; *see also* Affymetrix's Claim Construction Br. at 3, 6) Dependent claims 5, 8, and 9 further limit the claimed invention in terms of the length of the oligonucleotides ('432 claims 5 and 8) or the number of oligonucleotides ('432 claim 9).

II. The Poster Abstract: "Miniaturization of Sequencing by Hybridization (SBH): A Novel Method for Genome Sequencing"

In 1987, Drs. Crkvenjakov and Drmanac began working on an application of hybridization technology to determine the DNA sequence of genes, called Sequencing by Hybridization or SBH. (Ex. B, Drmanac Dep. Tr. at 12:3-19; Ex. C, Crkvenjakov Dep. Tr. at 67:14-68:6) In 1988, Drs. Crkvenjakov and Drmanac received a grant from the U.S. Department of Energy Human Genome Initiative to pursue their research on SBH. (Drmanac at 14:16-15:9,

41:21-42:1; Ex. D, Stodolsky Dep. Tr. at 23:9-25) The grant was funded under an international treaty that, among other things, fostered scientific collaboration with the United States by sponsoring visits to the United States for Drs. Crkvenjakov and Drmanac to report their progress at scientific meetings. (Stodolsky at 10:23-11:22, 23:9-25, 28:24-29:14, 74:17-75:4) Under this agreement, Drs. Crkvenjakov and Drmanac presented their research on SBH in posters and talks throughout the U.S., starting at the Wolf Trap Genome Sequencing Conference in Virginia on October 24-26, 1989 and the Human Genome Contractors/Grantee Workshop in Santa Fe, New Mexico on November 3-4, 1989. (Drmanac at 80:6-13, 81:13-21, 127:10-17; Crkvejakov at 83:1-84:12; Ex. E, Beattie Dep. Tr. at 47:10-19; 60:4-14) In particular, an abstract of their scientific poster presentation (Exs. F (Wolf Trap Poster Abstracts at IAFP00597869) and G (Santa Fe Workshop Abstracts at IAFP00597996)) was published in a booklet and distributed at the beginning of the Wolf Trap and Santa Fe conferences to all of the attendees, about 80 and 165 attendees, respectively (Ex. H (Wolf Trap Conference List of Attendees); Ex. I (Santa Fe Conference List of Attendees); Drmanac at 82:11-83:15, 127:18-128:22; Crkvenjakov at 78:6-82:2; Beattie at 46:16-47:3; Stodolsky at 73:12-23, 76:9-77:12; Ex. J, Mathies Dep. Tr. at 28:3-20).[3] This abstract highlighted Drs. Crkvenjakov and Drmanac's scientific poster presentations given at the conferences. (Drmanac at 84:1-20, 98:14-18, 127:10-129:9; Crkvenjakov at 78:6-15, 83:1-14; Stodolsky at 77:14-22, 80:19-81:11, 84:16-85:19; Beattie at 47:5-19)

In their poster abstract entitled "Miniaturization of Sequencing by Hybridization (SBH): A Novel Method for Genome Sequencing" (hereinafter referred to as "the SBH Abstract"), Drs. Crkvenjakov and Drmanac describe SBH as a method that uses short pieces of

[3] The abstracts from the Wolf Trap and Santa Fe conferences are the same. (Compare Ex. F at IAFP00597869 with Ex. G at IAFP00597996; *see* Crkvenjakov at 153:12-154:15)

DNA to identify the sequence of unknown DNA fragments. (Drmanac at 12:20-13:9) These short pieces of DNA, or oligonucleotides, are made up of a certain number of units, called nucleotides, that are joined together to form the length of the DNA piece. (*See* Affymetrix's Claim Construction Br. at 2) These oligonucleotides are used to identify the sequence of another piece of DNA through a process called hybridization that occurs as a result of the chemical nature of certain subunits of the nucleotide, known as bases, that have an affinity to bind with other bases: the base adenine ("A") binds with thymine ("T"); and cytosine ("C") binds with guanine ("G"). (*See id.* at 2-3) Based on these base pairings, the sequence of a piece of DNA can be determined by knowing the sequence of the complementary DNA sequence that has hybridized to it. (*See id.*)

Specifically, the SBH Abstract discloses that microscopic discrete particles, or beads, are randomly fixed in a monolayer to form an array that is to be used in a DNA sequencing analysis. (SBH Abstract; *see also* Ex. K, REDACTED

Two formats are described called "direct SBH" and "inverse SBH." (SBH Abstract) In direct SBH, DNA pieces to be analyzed are attached to the beads; whereas in inverse SBH, known oligonucleotide probes of a certain length of nucleotides, referred to generically as "n-mers," are attached to the beads.[4] (*Id.*) In inverse SBH, the SBH Abstract demonstrates how over 10 million different beads, each attached with a different oligonucleotide of 12 to 15 nucleotides (*i.e.* a "12-15mer"), are encoded with marker oligonucleotides of a unique combination. (*Id.*) These marker oligonucleotides are distinguished through repeated

[4] "n-mer" is the general description of the number of units that makes up the length of a polymer; in this case, the number of nucleotides. (*See* '432 col. 19:44-65 (referring to "ten nucleotide oligomers" as "10-mers"); Drmanac at 85:17-86:5 (referring to 12-15mers in the SBH Abstract as 12 to 15 nucleotide bases); *see also* Beattie at 51:19-52:3)

hybridization reactions to determine which 12-15mer is attached to which bead in the monolayer. (*Id.*)

The abstract explains that the method of using encoded beads to miniaturize SBH technology provides a highly efficient and scalable solution to sequencing the human genome. (*Id.*) The beads used as a solid support provide the vehicle to miniaturize the location of each oligonucleotide probe. (*Id.*) The encoding system allows the beads to be identified after they are assembled in a monolayer. Through the miniaturization of the location of the probes in an efficient assembly process, the number of analyses that could be performed at one time is greatly increased, and the SBH Abstract describes how a human DNA fragment could be sequenced in 1-100 hybridization reactions. (*Id.*)

Drs. Crkvenjakov[5] and Drmanac were both deposed in this case, and both confirmed in their depositions that Illumina is reading the SBH Abstract exactly as those of ordinary skill in the art would — to disclose all of the limitations of the relevant claims of the '432 patent. They walked through the SBH Abstract, explaining that their hybridization technology would be miniaturized by placing the oligonucleotides on microscopic discrete particles ("DPs"), or beads, so that a higher quantity of data sequences could be analyzed at one time. (Drmanac at 85:12-86:5; Crkvenjakov at 72:14-20, 108:25-109:7, 110:2-9, 111:5-18) Drs. Crkvenjakov and Drmanac confirmed that the abstract describes a collection of beads which have known oligonucleotide probes attached, by example, of 12 to 15 nucleotides long. (Drmanac at 87:11-25, 91:1-92:10) These oligonucleotide probes, or target specific sequences, bind with complementary oligonucleotides in an unknown DNA sample to determine the DNA

[5] Dr. Crkvenjakov is also serving as a consultant to Illumina in this case. (Crkvenjakov at 23:21-24:7)

sequence of that sample. (Drmanac at 91:10-92:10, 93:13-17) The beads themselves are encoded with an encoding system based on size, shape, color, or a marker oligonucleotide (an additional oligonucleotide of a unique sequence) in order to identify which probe is attached to which bead. (Drmanac at 86:6-87:10; Crkvenjakov at 108:25-109:7)

Indeed, other scientists working in the field of genomic sequencing, including a member of Affymetrix's Scientific Advisory Board, attended one or both of the conferences where the abstract was distributed and confirmed that one of ordinary skill in the art would read (and did read) the SBH Abstract to disclose every limitation of the asserted claims of the '432 patent. For example, Dr. Richard Mathies, Affymetrix's scientific advisor (Mathies at 7:13-25); Dr. Marvin Stodolsky, the DOE technical detailee for the Human Genome Initiative (Stodolsky at 10:4-22, 50:14-51:1); and Dr. Kenneth Beattie, a Professor of Biochemistry at Baylor (Beattie at 9:25-11:4), all received a publication of the SBH Abstract as attendees of either the Wolf Trap or Santa Fe conferences (Mathies at 28:3-28:20; Stodolsky at 77:6-13, 83:20-84:9; Beattie at 46:16-47:3). As persons of skill in the art, they each independently confirm that the SBH Abstract demonstrates a collection of beads with oligonucleotides of 12-15mers attached (Mathies at 34:3-15; Stodolsky at 55:12-57:19; Beattie at 47:20-24, 52:16-53:1), and that the beads are encoded with a unique marker oligonucleotide to determine which oligonucleotide probe is attached to which bead (Mathies at 34:16-35:6; Stodolsky at 59:16-25; Beattie at 47:25-48:18, 53:3-9).

Through their public presentations at Wolf Trap and Santa Fe, as well as at U.S. National Laboratories and other scientific conferences throughout the U.S. (Crkvenjakov at 83:1-84:12; Drmanac at 80:6-81:12), Drs. Crkvenjakov and Drmanac were recognized by others in the scientific community for their hybridization technology using encoded beads (Beattie at 80:11-

81:5 (referring to DX 276); *see also* Ex. L (DX 276 at IAFP00598052); Stodolsky at 53:10-54:9 (referring to DX 254); Ex. M (DX 254 at DOE 000470)).

REDACTED

ARGUMENT

Anticipation is appropriate for summary judgment where no genuine issue of material fact exists. *Telemac Cellular Corp. v. Topp Telecom, Inc.*, 247 F.3d 1316, 1327 (Fed. Cir. 2001) (affirming summary judgment of invalidity where "no reasonable jury could find" the patent valid in light of the prior art). A reference anticipates a claim if it discloses every limitation of the claimed invention, either expressly or inherently. *See Rapoport v. Dement*, 254 F.3d 1053, 1057 (Fed. Cir. 2001). "[T]he dispositive question regarding anticipation is whether one skilled in the art would reasonably understand or infer from the prior art reference's teaching that every claim [limitation] was disclosed in that single reference." *Akamai Technologies, Inc. v. Cable & Wireless Internet Services, Inc.*, 344 F.3d 1186, 1192-93 (Fed. Cir. 2003). If a reference contains every limitation of a claim, that claim is invalid as anticipated by that reference.

III. The SBH Abstract Anticipates Claims 2, 5, 8, and 9 of the '432 Patent

A. The SBH Abstract is Prior Art Under 35 U.S.C. § 102(b)

The SBH Abstract is prior art under 35 U.S.C. § 102(b) as a printed publication more than one year prior to the '432 patent's original filing date. Section 102(b) provides that:

> A person shall be entitled to a patent unless—
>
> * * *
>
> (b) the invention was patented or described in a ***printed publication in this or a foreign country*** or in public use or on sale

> in this country, ***more than one year prior to the date of the application for patent in the United States . . .***

"[P]ublic accessibility has been the criterion by which a prior art reference will be judged for the purposes of § 102(b)." *In re Klopfenstein*, 380 F.3d 1345, 1350-52 (Fed. Cir. 2004) (holding that a scientific poster presentation that was on display for three days, but not distributed, to those of ordinary skill in the art without confidentiality restrictions was a "printed publication" under § 102(b)). The test for determining whether a reference was publicly accessible is whether "it has been disseminated or otherwise made available to the extent that persons interested and of ordinary skill in the subject matter or art [] exercising reasonable diligence can locate it . . ." *Massachusetts Institute of Technology v. AB Fortia*, 774 F.2d 1104, 1109 (Fed. Cir. 1985) (holding a scientific paper delivered orally to those of ordinary skill in the art and distributed at least six times constitutes a "printed publication" for purposes of § 102). This test "may be met by distributing or making the [reference] available at a conference where members of the interested public were 'told of the [reference's] existence and informed of its contents.'" *Ajinomoto Co., v. Archer-Daniels-Midland Co.*, 1998 WL 151411 at *37 (D. Del. 1998) (citing *MIT*, 774 F.2d at 1109).

The SBH Abstract is a "printed publication" under 35 U.S.C. § 102(b). The SBH Abstract was published as part of a booklet of poster abstracts distributed to the attendees of the Wolf Trap Genome Sequencing Conference in Virginia and the DOE/NIH Human Genome Contractors/Grantee Workshop in Santa Fe. (Exs. F at IAFP00597869 and G at IAFP00597996; Crkvenjakov at 80:14-82:2, 154:25-155:22, 218:9-24, 225:9-25; Drmanac at 82:11-83:15, 127:18-128:22; Stodolsky at 76:9-77:13, 83:3-85:20; Mathies at 28:3-20) The SBH Abstract highlighted Drs. Crkvenjakov and Drmanac's poster presentation on the miniaturization of SBH using beads that was publicly displayed over the course of the conferences. (Drmanac at 98:14-

99:11, 100:17-101:6, 217:19-218:24, 219:25-221:16; Stodolsky at 77:14-22; Beattie at 73:8-24) Both the Wolf Trap and the Santa Fe conferences were held open to the public without any confidentiality restrictions, with attendees taking notes and pictures freely. (Stodolsky at 81:12-82:11, 86:17-88:4; Crkvenjakov at 221:3-9; Beattie at 44:18-45:21) In fact, these conferences were held specifically for the purposes of disseminating scientific information and facilitating collaborations related to nucleic acid hybridization and sequencing. (Crkvenjakov at 154:16-24, 217:23-218:8; Drmanac at 83:16-22; Beattie at 44:18-45:21; Stodolsky at 81:16-22, 86:17-87:2) The SBH Abstract was clearly distributed and presented to the interested scientific community (including a member of Affymax and Affymetrix's Scientific Advisory Board) without confidentiality restrictions, and therefore, constitutes a printed publication under § 102(b). *See MIT*, 774 F.2d at 1109.

The SBH Abstract is prior art under 35 U.S.C. § 102(b) as a printed publication published over one year prior to the date of the first application to which the '432 patent claims priority.

REDACTED

The SBH Abstract was published as of October 24, 1989, more than one year before December 6, 1990. (Ex. F, Wolf Trap Genome Sequencing Conference Book of Abstracts) The SBH Abstract, therefore, was a printed publication more than one year before the earliest application date, and constitutes prior art under 35 U.S.C. § 102(b).

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REDACTED

B. The SBH Abstract Discloses Every Limitation of Claims 2, 5, 8, and 9 of the '432 Patent

The SBH Abstract on its face anticipates claims 2, 5, 8, and 9 of the '432 patent. As set forth below, each and every limitation of the asserted claims of the '432 patent is disclosed in the SBH Abstract, as published at the Santa Fe conference on P37 (Ex. G at IAFP00597996) (line numbers inserted for citations to the SBH Abstract hereinafter):

MINIATURIZATION OF SEQUENCING BY HYBRIDIZATION (SBH): A NOVEL METHOD FOR GENOME SEQUENCING

Crkvenjakov, R., Drmanac, R., Strezoska Z., Labat I.,
Genetic Engineering Center, PO Box 794, 11000 Belgrade, Yugoslavia

Human genome sequencing based either on gel electrophoresis, or recently proposed hybridization (Drmanac et al. GENOMICS (1989) 4:114) methods requires automated equipment on macro scale and can not be imagined as a routine procedure. Macro scale is mandated due to the requirements of robotic positioning of samples on predetermined coordinates and polymer separation in gels. However, determination of oligonucleotide contents of DNA which underlies SBH theoretically allows the micro scale processes with micro separated samples altogether comprising a macro scale reaction. It is possible to use the determination which clone/probe is on which random micro position instead of placing clone/probe on predefined macro position or volume. We propose the use of micro discrete particles (DPs) as vehicles for samples/probes. The recognition of specific association of a DP and a clone/probe is achieveable by premarking of DPs and/or determining characteristics of clone/probe in situ. The most obvious ways of marking DPs are shape, size or color, or attaching to it a specific combination of known oligonucleotides. We offer two possibilities for human genome sequencing (Drmanac et al., manuscript in preparation). For direct SBH $1x10^7$ clones coming from 10 separate genome parts are bound to $1x10^6$ different DPs in as many macro reactions (or eventually in a single macro reaction). $1x10^9$ monolayers containing more than $1x10^7$ individual previously mixed DPs are each after DP identification hybridized with groups of 100 differently labeled octamers. To this end we have developed conditions for reliable short oligonucleotide hybridizations. For inverse SBH $1x10^{7-9}$ different DPs are prepared each carrying a unique 12-15mer and unique combination of 20 out of 40 marking oligos. No more than 5000 separate macro reactions are needed for their preparation. After 40 hybridizations with marker oligos to find association between 12-15mers and DPs in a monolayer, in 1-100 hybridizations with fragmented, end labeled human DNA data for sequencing are generated. The monolayer area covers at most 100 microscope slides. The data collection for both approaches needs automated image analysis giving speed of data bits acquisition of $1x10^8$/s. Finally a substantional computing has a major role to keep track of information and generate sequence (see accompanying abstract). The described miniaturization concept and ensuing savings make human genome sequencing immediately feasible in a laboratory pending technological development.

'432 patent claims 1, 2

'432 patent claim 1

'432 patent claims 2, 5, 8, 9

'432 patent claim 1

Claim 1: A collection of beads comprising . . .

'432 Claim Limitation	The SBH Abstract (Santa Fe P37)
1. A collection of beads comprising ...	"We propose the use of micro discrete particles (DPs) as vehicles for samples/probes." (lns. 14-15)
a plurality of beads which have binding polymers of different target specific sequence attached thereto;	"[D]etermination of oligonucleotide contents of DNA [] underlies SBH . . ." (lns. 7-8) "For inverse SBH, $1x10^{7-9}$ different DPs are prepared each carrying a unique 12-15mer and unique combination of 20 out of 40 marking oligos." (lns. 29-32)
said beads being coded with an encoding system whereby the target specific sequence of the polymer attached to the beads can be identified.	"The recognition of specific association of a DP and a clone/probe is achievable by premarking of DPs and/or determining characteristics of clone/probe in situ. The most obvious ways of marking DPs are shape, size or color, or attaching to it a specific combination of known oligonucleotides." (lns. 15-20)

REDACTED

REDACTED

REDACTED The SBH Abstract describes an "inverse SBH" format that uses target specific sequences, or known DNA sequences (12-15mers), attached to beads to determine the sequence of an unknown DNA sample. (lns. 7-11, 29-32; *see also* Drmanac at 87:18-25, 91:10-92:10) And one need look no further than the use of the plural form of discrete particles to see that the SBH Abstract discloses two or more beads, which is all that is required by claim 1. Under either parties' claim construction,[7] therefore, this limitation is present in the SBH Abstract.

REDACTED

The SBH Abstract describes how the attached sequence can be identified by its association with a "premarked," or encoded, bead. (lns. 15-18; Crkvenjakov at 108:25-109:7; Drmanac at 85:17-86:12, 88:1-9) The abstract explains various methods to encode the bead are by "shape, size or color, or attaching to it a specific combination of known oligonucleotides." (lns. 18-20). As can be seen, the SBH Abstract therefore not only describes encoding systems, but the ***exact same embodiments*** of encoding systems set forth (more than a year later) in the '432 patent. There can be no dispute that the SBH Abstract discloses each and every element of claim 1 of the '432 patent.

[7] Illumina proposed "target specific sequence" be construed as "a known sequence of a polymer that binds with specificity to the target at the sequence to be determined." (D.I. 240 at 18) Affymetrix proposed that "target specific sequence" is to be construed as "a known polymer sequence that has affinity for another sequence." (D.I. 243 at 13) The SBH Abstract discloses oligonucleotide probes that bind with a target to be sequenced. This description satisfies both parties' proposed constructions, and therefore, the SBH Abstract satisfies this limitation.

Claim 2: The collection of claim 1, wherein the binding polymer is an oligonucleotide having a given length and is selected from the group consisting of all possible oligonucleotide sequences having the same number of nucleotides.

'432 Claim Limitation	The SBH Abstract (Santa Fe P37)
2. The collection of claim 1, wherein the binding polymer is an oligonucleotide having a given length and is selected from the group consisting of all possible oligonucletide sequences having the same number of nucleotides.	"[D]etermination of oligonucleotide contents of DNA [] underlies SBH . . ." (lns. 7-8) "For inverse SBH, $1x10^{7-9}$ different DPs are prepared each carrying a unique 12-15mer and unique combination of 20 out of 40 marking oligos." (lns. 29-32)

The SBH Abstract also discloses a collection of beads with "oligonucleotides of [the same] given length" as required in claim 2. The plain language of this claim requires that the sequences attached to the collection of beads are oligonucleotides of all the same length. The SBH Abstract describes by example a collection of beads with oligonucleotide probes of given lengths. (lns. 29-32; *see also* lns. 7-15) In the example, "$1x10^{7-9}$ different DPs [at least 10 million beads] are prepared each carrying a unique 12-15mer . . . ." (lns. 29-32) This example allows for at least 10 million beads with any combination of 12-, 13-, 14- and 15mers attached.[8] (*See, e.g.*, Drmanac at 90:7-14) Because the example suggests four distinct lengths of 12, 13, 14, or 15 nucleotides can be used for at least 10 million beads, there would be at least two beads with the same length oligonucleotide attached to them; in fact, by necessity there must be at least 2.5 million beads with the same length oligonucleotide attached.[9] Therefore, the SBH Abstract

[8] By this example, the SBH Abstract also anticipates claim 22, which appears to require a collection of beads with oligonucleotide probes of different lengths attached. ('432 claim 22) Because Affymetrix attempted to assert this claim only after fact discovery closed, however, Illumina has not been able to conduct any discovery related to claim 22. If the Court permits Affymetrix to add this claim, Illumina requests the opportunity for further briefing to seek summary judgment that claim 22 is invalid.

[9] For example, the collection of 10 million beads could have all oligonucleotides of the same length, such as 12mers, attached. Alternatively, the collection of 10 million beads could have oligonucleotides of all four lengths, with each length attached to a minimum (by dividing equally) of 2.5 million beads, resulting in a collection of 2.5 million 12mers, 2.5 million 13mers, 2.5 million 14mers, and 2.5 million 15mers. With four different suggested (Continued...)

example requires that more than one bead carry the same length oligonucleotide, and satisfies the limitation of a collection of beads with the same length oligonucleotides attached thereto. The SBH Abstract, therefore, anticipates claim 2 of the '432 patent.

Claims 5 and 8: The collection of claim 2, wherein the oligonucleotide sequences having the same number of nucleotides are at least 5 and 10 nucleotides long.

'432 Claim Limitation	The SBH Abstract (Santa Fe P37)
5. The collection of claim 2, wherein the oligonucleotide sequences having the same number of nucleotides are at least 5 nucleotides long.	"For inverse SBH, $1x10^{7-9}$ different DPs are prepared each carrying a unique 12-15mer and unique combination of 20 out of 40 marking oligos." (lns. 29-32)
8. The collection of claim 2, wherein the oligonucleotide sequences having the same number of nucleotides are at least 10 nucleotides long.	

The SBH Abstract further discloses a collection of beads with "oligonucleotides sequences having the same number of nucleotides are at least 5 [or 10] nucleotides long" as required in claims 5 and 8, respectively. The plain language of these claims require that the oligonucleotides attached to the collection of beads are all the same length and at least 5 or 10 nucleotides long. The SBH Abstract describes 12-15mers, or oligonucleotides of 12-15 nucleotides long, attached to a collection of beads, satisfying either the 5 or 10 nucleotides long limitiation. (lns. 29-32) The SBH Abstract thus anticipates claims 5 and 8 as well.

lengths to attach to a minimum of 10 million beads, one of these lengths, therefore, must be used to attach to 2.5 million beads or more.

Claim 9: The collection of claim 2, wherein at least 10,000 of all the possible oligonucleotide sequences having the same number of nucleotides are each attached to a different single bead.

'432 Claim Limitation	The SBH Abstract (Santa Fe P37)
9. The collection of claim 2, wherein at least 10,000 of all the possible oligonucleotide sequences having the same number of nucleotides are each attached to a different single bead.	"For inverse SBH, $1x10^{7-9}$ different DPs are prepared each carrying a unique 12-15mer and unique combination of 20 out of 40 marking oligos." (lns. 29-32)

The SBH Abstract further discloses a collection of beads with "at least 10,000 of all the possible oligonucleotide sequences having the same number of nucleotides [] each attached to a different single bead" as required in claim 9. The plain language of this claim requires that at least 10,000 oligonucleotide sequences of the same length are each attached to a different bead. The SBH Abstract describes between 10 million and 1 billion different beads, "each carrying a unique 12-15mer . . . ." (lns. 29-32) Given that the goal of the SBH Abstract is to sequence the human genome, the description of this range of 12 to 15 nucleotides would require the use of the majority, if not all, combinations of oligonucleotides of these lengths. (Drmanac at 89:12-90:6) In fact, the SBH Abstract further describes how human DNA can be sequenced in "1-100 hybridizations."[10] (lns. 33-36) Using the minimum criteria described in the SBH Abstract, for example, simple math confirms that there are over 16 million unique 12mers,[11] more than enough to cover the 10 million beads described. (*See, e.g.*, Drmanac at

[10] With this description, the SBH Abstract also anticipates claim 21, which appears to require that the plurality of beads of claim 2 is "reusable," or capable of being used for subsequent hybridization with target polynucleotides. ('432 claim 21; col. 25:6-10) The SBH Abstract describes how the monolayer of beads with oligonucleotide probes is used for sequencing human DNA in "1-100 hybridizations," indicating how the beads are reusable for subsequent hybridizations with target DNA, and thus anticipates claim 21. (lns. 33-36) Because Affymetrix attempted to assert this claim only after fact discovery closed, however, Illumina has not been able to conduct any discovery related to claim 21. If the Court permits Affymetrix to add this claim, Illumina requests the opportunity for further briefing to seek summary judgment that claim 21 is invalid.

[11] The formula to calculate all possible number of n-mers containing a unique combination of the 4 possible nucleic acid bases is 4^n. (*See* '432 col. 15:1-14) Specifically, the total number of all possible 12mers is 4^{12} or 16,777,216.

92:19-93:12) This example of 16 million 12mers attached to a collection of at least 10 million beads, therefore, more than satisfies the limitation of at least 10,000 oligonucleotides of the same length, each attached to a different bead.[12]

C. Testimony of Those of Skill in the Art Confirm the SBH Abstract Anticipates Claims 2, 5, 8, and 9 of the '432 Patent

Testimony from several scientists that attended the Wolf Trap and Santa Fe conferences confirm that the SBH Abstract anticipates claims 2, 5, 8, and 9 of the '432 patent.

REDACTED

Dr. Marvin Stodolsky was a technology leader for the Department of Energy, promoting research opportunities to sequence the human genome by serving as a technical representative to the DOE for various research grantees, including Drs. Crkvenjakov and Drmanac. (Stodolsky at 7:7-18, 10:4-22, 50:3-51:1) Dr. Kenneth Beattie was a Professor of Biochemistry at Baylor at the time, and has since retired from Oak Ridge National Laboratory. (Beattie at 9:25-11:4) Each one separately confirms, as one of skill in the art, that the SBH Abstract discloses every limitation of claims 2, 5, 8, and 9 of the '432 patent.

In general, the SBH Abstract describes a method of SBH to sequence DNA using known oligonucleotides probes, or target specific oligonucleotides. (Mathies at 33:21-34:8;

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[12] For the same reasons described with regard to claim 9, the SBH Abstract also anticipates claim 10. The example of 16 million 12mers attached to a collection of at least 10 million beads satisfies the limitation of claim 10, which requires at least 100,000 oligonucleotides of the same length, each attached to a different bead. ('432 claim 10) Because Affymetrix attempted to assert this claim only after fact discovery closed, however, Illumina has not been able to conduct any discovery related to claim 10. If the Court permits Affymetrix to add this claim, Illumina requests the opportunity for further briefing to seek summary judgment that claim 10 is invalid.

[13] Affymax is predecessor-in-interest to Affymetrix, and thus was the relevant entity at the time of the conferences and the purported invention of the '432 patent.

Beattie at 53:17-23; *cf.* '432 claim 1) These probes are attached to discrete particles, understood by one of ordinary skill in the art to include beads. (Mathies at 34:9-15; Stodolsky at 55:12-57:19 (equating "discrete particles" with "beads")[14]; Beattie at 47:20-24; *cf.* '432 claim 1) The SBH Abstract also describes to one of ordinary skill in the art how the beads are encoded to recognize which probe is attached to which bead, marked by size, shape, color, or by attaching a specific combination of known oligonucleotides. (Mathies at 34:16-35:6; Stodolsky at 59:16-25; Beattie at 47:25-48:18, 53:3-9; *cf.* '432 claim 1)

By example, the SBH Abstract further describes "$1x10^{7-9}$ different DPs [] each carrying a unique 12-15mer and unique combination of 20 out of 40 marking oligos" (lns. 29-32), disclosing to one of ordinary skill in the art "a collection of beads" containing "binding polymers with different target specific oligonucleotides" of 12-15mers attached (Beattie at 52:16-53:23; *cf.* '432 claims 1, 2, 5, 8).

REDACTED

It is clear that the SBH Abstract discloses each and every limitation of claims

[14] Dr. Stodolsky served as Drs. Crkvenjakov and Drmanac's technical representative to the DOE and made personal visits to their labs to learn about their research on SBH. (Stodolsky at 50:3-51:1; 28:12-29:24, 41:16-22) Dr. Stodolsky confirms that the SBH Abstract reflects Drs. Crkvenjakov and Drmanac's research on SBH using discrete particles. (Stodolsky at 85:12-20) Therefore, citations refer to Dr. Stodolsky's understanding of Drs. Crkvenjakov and Drmanac's work regarding the same language that appears in the SBH Abstract.

2, 5, 8, and 9 of the '432 patent to one of ordinary skill in the art and anticipates the '432 patent as a matter of law.

CONCLUSION

For all the reasons set forth herein, no material issues of fact exist, and Illumina respectfully requests that this Court grant its motion for summary judgment and enter its proposed order granting summary judgment that claims 2, 5, 8, and 9 of the '432 patent are invalid under 35 U.S.C. § 102.

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CERTIFICATE OF SERVICE

I hereby certify that on this 16th day of August, 2006, I caused to be electronically filed the foregoing document, **REDACTED VERSION OF THE OPENING BRIEF IN SUPPORT OF ILLUMINA'S MOTION FOR SUMMARY JUDGMENT OF INVALIDITY OF THE ASSERTED CLAIMS OF THE '432 PATENT**, with the Clerk of the Court using CM/ECF which will send notification of such filing to the following:

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Additionally, I hereby certify that on this 16th day of August, 2006, the foregoing document was served via email on the following non-registered participant:

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